REMARKS / ARGUMENTS

In response to the Office Action of May 29, 2008, Applicants respectfully request the Examiner reconsider and withdraw the rejection of claims in this application.

Claims 11-12, 15 and 17 have been rejected under 35 U.S.C.§ 102(b) as allegedly anticipated by Gregory et al. US 5,283,257. Gregory et al. has been cited for allegedly teaching at column 5, lines 20-37, a method of inhibiting hyperproliferative vascular diseases by administering rapamycin and mycophenolic acid. According to the Examiner, "the reference further teaches other agents such as cyclosporine A and FK-506 are used in combination, see col. 5, lines 30-37 as required by instant claims 12 and 15." Office Action, page 3.

Applicants respectfully submit that the Gregory et al. reference utilizes rapamycin in combination with mycophenolic acid. The presently claimed 40-O-(2-hydroxy)ethyl-rapamycin derivative is nowhere mentioned in Gregory et al. Applicants further respectfully submit that the Gregory et al. reference does not teach the combination of cyclosporin A and FK-506 as the Examiner has asserted. Rather, Gregory et al. teaches five different treatments: (1) cyclosporin, (2) FK506, (3) mycophenolic acid (MPA) and (5) a combined treatment of rapamycin plus MPA. *See* Gregory et al., column 5, lines 20-44, Table 1, and Figure 3. Claims 11-12, 15 and 17 are therefore distinguished from the teaching of Gregory et al., and withdrawal of the rejection of claims 11-12, and 15 under 35 U.S.C.§ 102(b) is warranted.

Claims 11-19 have been rejected under 35 U.S.C. §103(a) as allegedly obvious over Gregory et al. (US 5,283,257) and Fraser-Smith et al. (1995) *J. Pharmacology and Experimental Therapeutics 275*(3):1204-1208, in view of Pichard et al. (1996)

Biochemical Pharmacology 51:591-598, Goldberg, US 5,364,612 and de Boer et al. US 5,747,034.

Gregory et al. has been cited for allegedly teaching a method of inhibiting hyperproliferative vascular diseases by administering rapamycin and mycophenolic acid. *See* column 5, line 66, to column 6, line 1. The Examiner has acknowledged that Gregory et al. fails to teach the use of other agents such as Cyclosporin G, and mycophenolate mofetil.

Fraser-Smith et al. has been cited for allegedly teaching the administration of mycophenolate mofetil to suppress thickening caused by vascular injury.

Pichard et al. has been cited for allegedly teaching that cyclosporin G is structurally similar and pharmacologically active to cyclosporine A but less toxic. The Examiner has asserted that therefore, one skilled in the art would be motivated to use a less toxic drug having the same activity for the treatment of the same type of disease condition.

Goldenberg has been cited for allegedly teaching targeting cardiovascular lesions such as atherosclerotic plaques with an antibody imaging agent such as CD1-8. It is the position of the Examiner that in order for treatment to be done, detection must also be done. Office Action, page 4.

The de Boer et al. reference has been cited for allegedly teaching the administration of CTLA4Ig with rapamycin for the treatment of chronic graft rejection. The Examiner has specifically cited column 14, lines 50-67 for this teaching. According to the Examiner, since immunosuppressive agents are known to inhibit proliferation of T cells, "one of ordinary skill in the art would be motivated to use these compounds because these compounds inhibit proliferation in graft transplant." It is the further position of the Examiner that one of skill in the art would be motivated to combine the cited references to treat neointimal proliferation or chronic organ rejection because these

agents are known in the art for the treatment of restenosis/neointimal proliferation from vascular injury. Office Action, page 5.

Applicants respectfully traverse the rejection for the following reasons. In the first instance, the present claims are directed to inhibiting or treating neointimal proliferation and thickening and/or restenosis and/or vascular occlusion following vascular injury. Inhibiting or treating chronic rejection is not recited by the present claims.

It is further respectfully submitted that one skilled in the art would not be motivated to combine the references in the manner the Examiner has done, and even if the references were combined, one skilled in the art would still not have arrived at the presently invention.

Applicants respectfully submit that Gregory et al. fails to teach the presently claimed 40-O-(2-hydroxy)ethyl-rapamycin in combination with mycophenolic acid, or any other combination treatment.

Fraser-Smith et al. does not add anything to the teaching of Gregory et al., since it is limited in teaching the use of mycophenolate-mofetil alone to suppress thickening caused by vascular injury.

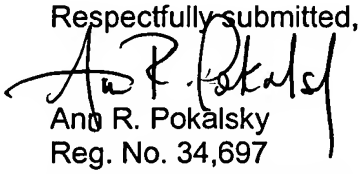
In teaching that cyclosporin G might be substituted for cyclosporin A, Pichard et al. does not add anything to the dearth of teaching provided by Gregory et al. and Fraser-Smith et al.

Goldenberg also adds nothing to the combined teachings of Gregory et al. and Fraser-Smith in view of Pichard et al., since Goldenberg is limited to methods for *targeting* and early *imaging* of cardiovascular lesions using an antibody or antibody fragment which binds to at least one type of leukocyte and also selectively binds to at least one antigen associated with fibrin, myosin or platelets. Indeed, one skilled in the art in devising a treatment method, would not likely consider the teachings of Goldenberg, which are directed to diagnostic methods.

Finally, de Boer et al. does not cure the deficiency of teachings provided by Gregory et al., Fraser-Smith et al., Pichard et al. and Goldenberg. Applicants' position is predicated on de Boer et al. being concerned with methods of preventing or treating transplant rejection, graft versus host disease, and other immunological conditions arising from the recognition of specific antigens as foreign. *See* column 1, lines 10-15. Accordingly, the rejection of claims 1-10 under 35 U.S.C. §103(a) should be withdrawn.

In view of the foregoing remarks, it is firmly believed that the present application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



Ann R. Pokalsky
Reg. No. 34,697
Attorney for Applicants

DILWORTH & BARRESE
333 Earle Ovington Blvd.
Uniondale, NY 11553
(516) 228-8484
ARP/ml/sbs